

# Neonatal pneumothorax in association with APGAR score: A systematic review and meta-analysis

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**ABSTRACT**

**Introduction:** Pneumothorax (PTX) is a potentially fatal condition that primarily affects neonates. Premature babies are more likely to have underlying lung diseases, such as respiratory distress syndrome (RDS), which increases the risk of air leakage. **Methodology:** This was a systematic review and meta-analysis to estimate the association between neonatal PTX and Apgar score. A systematic electronic search was implemented through Google Scholar, PubMed, Web of Science, Science Direct, and EBSCO to include the eligible studies. **Results:** A total of 5 studies were included, with 357 patients (135 cases and 222 controls). The estimated association between the 5-minutes APGAR score and Neonatal PTX was [SMD=-0.91, (95% CI; -1.49, -0.33), P=0.002] and [SMD=-0.71,(95% CI; -1.01, -0.40), P=0.000] with the 1-minute APGAR score. **Conclusion:** We demonstrated a significant association between 1-minute and 5-minutes APGAR scores and neonatal PTX. The highest risk was found among neonates admitted to the ICU and those with persistent PTX.

**Keywords:** Neonatal pneumothorax; APGAR score; PTX; neonates.

**1. INTRODUCTION**

Pneumothorax (PTX) is a life-threatening illness that most frequently affects newborns (Boo & Cheah, 2011). A PTX is a collection of air in the pleural space that can cause clinically significant consequences such as hypoxemia, increased effort of breathing, hypercapnia, the need for evacuation, obstructive shock, hypotension, and sometimes even death (Gomella et al., 2013 & Smith et al., 2011). PTX rates are highest during the newborn period, with estimates ranging from 0.05% to 0.1% of all live births. The reported

incidence of radiographic diagnosis of PTX in cohorts of term and late preterm infants ranges from 1% to 2%. Due to obstetrical, perinatal, prognosis, and care measures, rates may vary (Smith et al., 2011). Prematurity is a known risk factor for PTX, with late preterm neonates (34–36 weeks GA) having a greater rate of PTX than term neonates (Bhatia et al., 2011 & Kitsommart et al., 2009). Preterm infants are more likely to have underlying lung illnesses, including respiratory distress syndrome (RDS), which raises the risk of air leakage (Kitsommart et al., 2009).

Positive pressure ventilation, meconium aspiration, vigorous resuscitation, male sex, and being larger are all risk factors for PTX in term newborns (Katar et al., 2006; Al Tawil et al., 2004; Benterud et al., 2009). Caesarean delivery (Katar et al., 2006 & Al Tawil et al., 2004) and birth outside of a tertiary perinatal centre have been indicated as risk factors for PTX, but the data is inconsistent. Furthermore, most prior PTX studies (Katar et al., 2006; Al Tawil et al., 2004; Benterud et al., 2009) were conducted in single locations with small sample sizes and insufficient statistical power. The influence of PTX on other clinically relevant outcomes, including broncho-pulmonary dysplasia (BPD), severe intra-ventricular haemorrhage (IVH, grade III or more), and duration of NICU stay, has been inconsistent or missing (Bhatia et al., 2011; İlçe et al., 2003; Esme et al., 2008).

The Apgar score was developed by Dr Virginia Apgar, an anesthesiologist at Columbia University, in 1952. The score is a rapid way to evaluate a newborn shortly after birth and in response to resuscitation. The American College of Obstetricians and Gynaecologists and the American Academy of Paediatrics recommend Apgar score as an assessment technique. Whereas Apgar scores were originally intended to assess the need for intervention to demonstrate breathing at 1 minute, the Neonatal Resuscitation Program (NRP) protocols state that they do not define the initial need for intervention because resuscitation must be started before the 1-minute Apgar score is allocated (Ayrapetyan et al., 2019; Medeiros et al., 2018; Yeagle et al., 2018). Colour, heart rate, reflexes, muscular tone, and respiration are all factors in the Apgar score. Apgar scoring is used to determine whether cyanosis, hypoperfusion, bradycardia, hypotonia, respiratory failure, or apneas are symptoms of hemodynamic compromise. Each element is given a score of 0 (zero), 1 (one), or 2 (two). All infants' scores are documented at 1 minute and 5 minutes, with extended recording at five-minute intervals for infants who score seven or less at 5 minutes and those who require resuscitation as a way of response monitoring. Scores of seven to ten are regarded as reassuring (Simon et al., 2021).

In addition, the Apgar score has its own set of limitations. Drugs, trauma, congenital defects, infections, hypoxia, hypovolemia, and preterm birth are among variables that might affect an Apgar score. There are little reliable data on the importance of the Apgar score in preterm infants up to this point. Because parts of the score such as tone, colour, and reflex irritability are influenced by the infants' physiologic maturity, a healthy preterm infant with no signs of hypoxia may have a lower score mainly due to immaturity. This systematic review and meta-analysis aimed to assess the association between neonatal PTX and Apgar scores.

## 2. METHODOLOGY

### **Study design and duration**

This systematic review and meta-analysis were conducted between Abril and May 2021.

### **Study condition**

This study mainly investigates the published relevant literature of the association between neonatal PTX and 1-minute APGAR score and 5-minutes APGAR score.

### **Search strategy**

An electronic systematic literature search of five major databases, Google Scholar, PubMed, Web of Science, Science Direct, and EBSCO, was implemented to comprise relevant and eligible literature. The search process was restricted to the English language and each database as necessary. The relevant literature was identified through the following keywords that conformed into Mesh terms in PubMed or subject terms as in EBSCO; "Neonatal pneumothorax," "PTX," "neonates," "newborns," "APGAR score," "1-minute APGAR score," and "5-minutes APGAR score". Boolean operators like "OR" and "AND" were combined with the proper keywords. Full texts, freely accessible papers, human trials, and the English language were included in the search results.

### **Selection criteria**

This review included the studies with the following criteria:

Original study articles that investigate the association between neonatal PTX and APGAR score.

Only newborns were included in this study.

Exclusion criteria comprised the following:

Studies that are not conducted in English

When there is no free access to the studies.

#### **Data extraction**

The duplicate evaluation parts of the search strategy results were determined using Rayyan (QCRI) (Ouzzani et al., 2016). By evaluating the pooled search results using a set of inclusion/exclusion criteria, the researchers looked for titles and abstracts that were convenient. The reviewers evaluated the whole text of the papers that met the inclusion criteria. Any disagreements amongst the authors were resolved through debate and discussion. A data extraction form was designed to contain the eligible studies. Study titles, authors, study year, study design, study population, participant number, participant age (age range, mean age, or median age), and gender were all extracted by the authors, the mean 1-minute and 5-minutes APGAR scores in neonates with and without PTX and.

#### **Risk of bias assessment**

The Newcastle-Ottawa Scale (NOS) (Wells et al., 2000) was used for qualitative and quantitative data synthesis for case-control, cohort, and cross-sectional studies to assess the included research quality. The reviewers explored and debated any conflicts in the quality evaluation. The funnel diagram was inspected visually to establish publication bias.

#### **Strategy for data synthesis**

To provide a qualitative overview of the included research aspects and outcome data, summary tables containing the collected details from the eligible studies were presented. After the data processing was evaluated, the scope of the recommended pooled analysis was examined. After the data extraction in this meta-analysis was completed, decisions were made about how to better use case and control data. A qualitative synthesis of the determined data was carried out, regardless of the validity of the pooled meta-analyses. Studies that fulfilled the full-text criteria but did not provide numerical data on the APGAR score in neonatal PTX patients were excluded.

The authors used Review Manager 5.4 (Cochrane Collaboration, 2020) to perform quantitative data synthesis for the condition of interest analyses. The effect of 1-minute and 5-minutes APGAR scores on neonates with PTX was assessed using random-effects meta-analysis. Heterogeneity was evaluated using an I-square statistic as part of the pooled meta-analysis. To quantify publication bias, the funnel-plot and funnel-plot symmetry measurements were utilised.

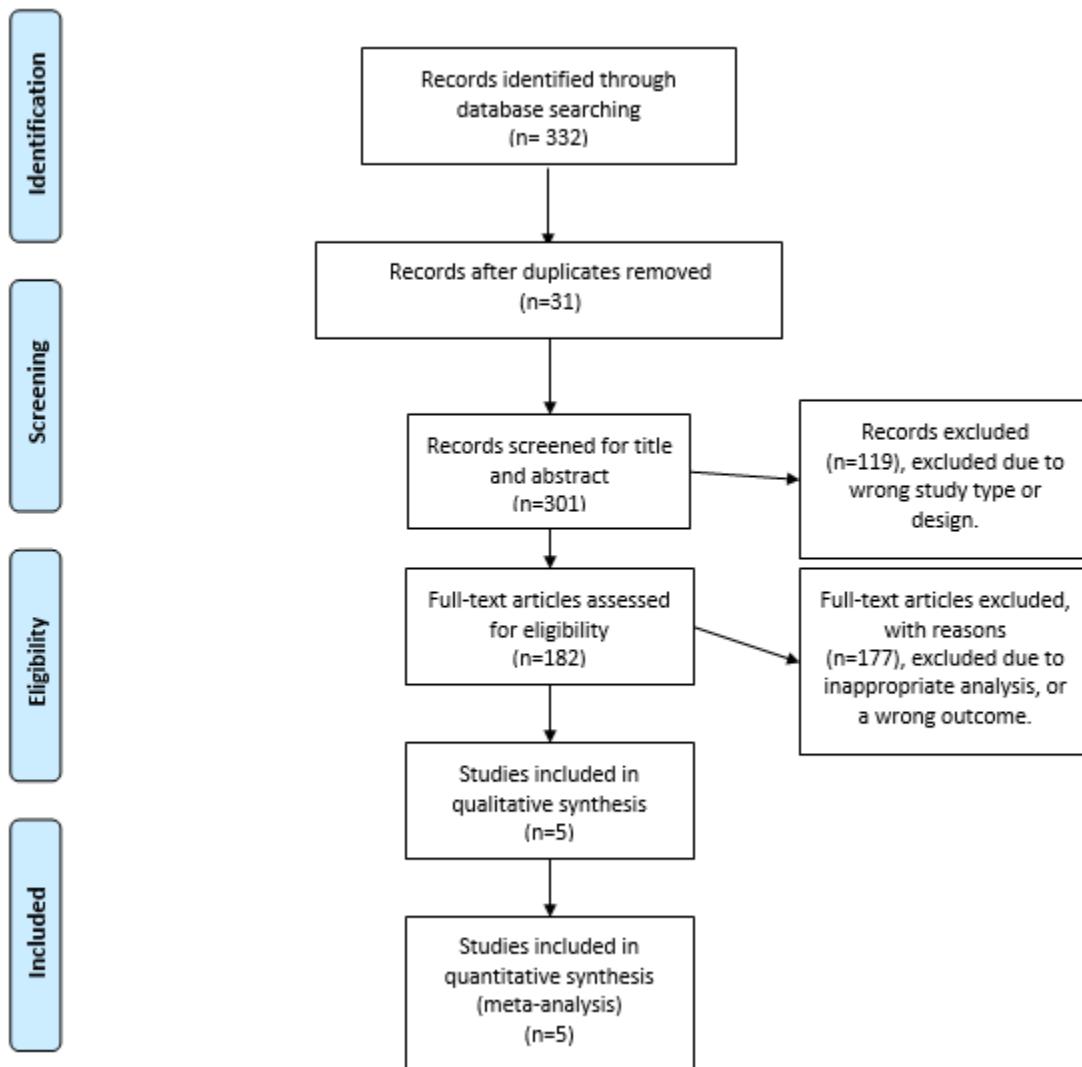
### **3. RESULTS**

#### **Search results**

A total of 332 study articles were identified from the initial systematic search. Of these studies, 31 duplicate records were determined and removed. Additionally, 119 studies were excluded after the title and abstract screening. Following the full-text assessment of the remaining studies, 177 articles were excluded due to wrong population type, wrong outcome and not available access for articles. Then only 5 unique studies were eligible and included for the final analysis, with a total of 357 neonates with PTX (135 cases and 222 controls). A summary of the search process is illustrated in Figure 1.

#### **Characteristics of the included studies**

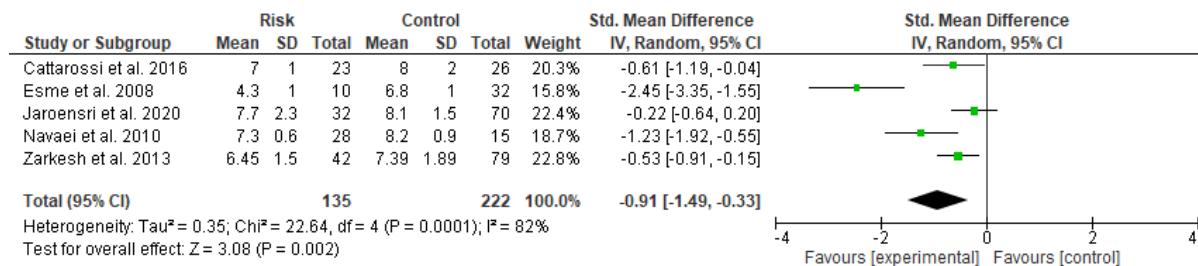
Of the included 5 studies, 2 studies were conducted in Iran (Zarkesh et al., 2013 & Navaei et al., 2010), one in Thailand (Jaroensri et al., 2020), one in Italy (Cattarossi et al., 2016), and one in Turkey (Litmanovitz et al., 2008). Zarkesh et al., (2013) included neonates with PTX in premature birth weight under mechanical ventilation. Jaroensri et al., (2020) included new borns with PTX associated with persistent pulmonary hypertension. Cattarossi et al., (2016) and Esme et al., (2008) both included neonates with PTX. Navaei et al., (2010) included neonates with PTX admitted to the ICU. Characteristics of the eligible study articles are presented in Table 1.

**Figure 1** PRISMA flowchart showing the selection process of eligible study articles.**Table 1** Characteristics of the eligible study articles

Study	Study design	Population type	Participants (n)	Case (n)	Control (n)	Age	Males (n)	Males (%)	Country	Apgar (5 mins)	Control	Apgar (1 min)	Control	NOS
Zarkesh et al. 2013 [22]	Cross-sectional	PTX in premature low birth weight infants who underwent mechanical ventilation	121	42	79		65	53.7	Iran	6.45 ±1.5	7.39±1.89			6
Jaroensri et al. 2020 [24]	Retrospective case-control	Newborns with pneumothorax associated with persistent pulmonary hypertension	102	32	70		70	68.8	Thailand	7.7±2.3	8.3±1.5	6±3.1	7.6±2.3	7
Cattarossi et al. 2016 [25]		Neonates with Pneumothorax	49	23	26				Italy	7 ± 1	8 ± 2	4 ± 4	6 ± 2	7
Esme et al. 2008 [13]	Retrospective study	Neonates with persistent pneumothorax	42	10	32	30-43	26	61	Turkey	4.3±1	6.8±1			8
Navaei et al. 2010 [23]	Retrospective study	Pneumothorax in neonatal ICU	43	28	15				Iran	7.3±0.6	8.2±0.9	5.6±0.9	6.7±1.3	6

**PTX in association with 5-minute APGAR Score**

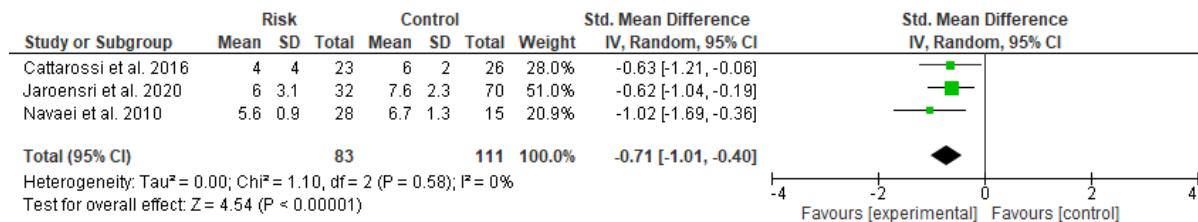
The estimated association between the 5-minutes APGAR score and Neonatal PTX was [SMD=-0.91,(95% CI; -1.49, -0.33), P=0.002], which indicates that a low 5-minutes APGAR score was significantly associated with a higher risk of developing neonatal PTX. Moreover, significant heterogeneity was demonstrated ( $I^2=82\%$ ). These findings are presented using a random-effects model meta-analysis in (Figure 2).



**Figure 2** Forest Plot of the association between 5-minutes APGAR score and neonatal PTX.

**Neonatal PTX in Association with 1-minute APGAR Score**

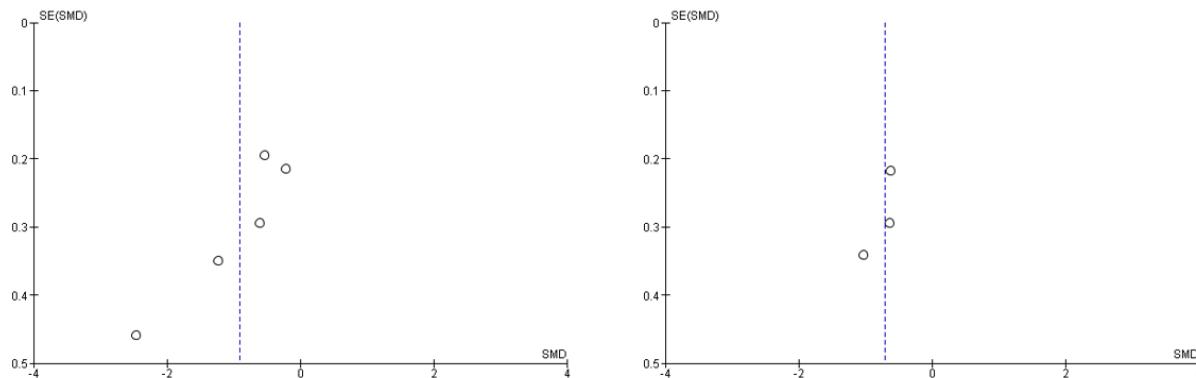
The estimated association between the 1-minute APGAR score and Neonatal PTX was [SMD=-0.71,(95% CI; -1.01, -0.40), P=0.000]. This also indicates that a low 1-minute APGAR score was significantly associated with a higher risk for neonatal PTX. Moreover, no significant heterogeneity was demonstrated between the studies ( $I^2=0\%$ ). These findings are presented using a random-effects model meta-analysis in (Figure 3).



**Figure 3** Forest Plot of the association between 1-minute APGAR score and neonatal PTX.

**Inter-study heterogeneity and publication bias**

Visual inspection of funnel plots reveals an almost symmetrical distribution of the SMDs for both, 5 minutes APGAR score data (figure 4a), and 1 minute APGAR score data (figure 4b). The Higgins'  $I^2$  test was used to assess data for inter-study heterogeneity. Figure 2 shows significant heterogeneity for data regarding 5 minutes APGAR score ( $I^2=82\%$ , P=0.0001), whereas figure 3 on PTX association with 1 minute APGAR score shows no significant heterogeneity.



a) 5 Minutes APGAR Score

b) 1 Minute APGAR Score

**Figure 4** Funnel plots for publication bias.

## 4. DISCUSSION

PTX in newborns is a life-threatening disorder with a high death and morbidity rate (Litmanovitz & Carlo, 2008). Despite the high prevalence, only 0.5% of PTX incidents are symptomatic. The occurrence of a PTX and the resulting hypoxia and hypercapnia are potentially fatal (Mannan et al., 2019; Apiliogullari et al., 2011). In this systematic review and meta-analysis, the APGAR score was investigated as a potential risk factor for neonatal PTX.

The current study demonstrated a significant association between 5-minutes APGAR score and neonatal PTX [SMD=-0.91, (95% CI; -1.49, -0.33)]. The highest risk was reported by Esme et al., (2008) among neonates with persistent PTX[SMD=-2.45, (95% CI; -3.35, -1.55)]. The side of PTX, Apgar score, using mechanical ventilation, and preexisting primary lung pathology all had a significant relationship with death, but not with APGAR score and accompanying disorders. They also reported that the APGAR score at 5-minutes is a critical parameter in newborn evaluation. Only 12% of survivors had low Apgar readings, while 50% of non-survivors had poor Apgar scores (Esme et al., 2008).

Navaei et al. (2010) also recorded high risk of 5-minutes APGAR score among neonates admitted at the ICU unit with PTX [SMD=-1.23, (95% CI; -1.92, -0.55)]. These results may interpret the higher need for neonatal resuscitation among patient groups with lower 5-minutes APGAR score. However, the lowest risk regarding the 5-minutes APGAR score and neonatal PTX was found in newborns with PTX associated with persistent pulmonary hypertension [SMD=-0.22, (95% CI; -0.64, 0.20)] (Jaroensri et al., 2020). They suggested that lower APGAR scores are linked to patients receiving mask and bag ventilation, which increases the risk of PTX (Jaroensri et al., 2020).

This study found a significant association between 1-minute APGAR score and neonatal PTX [SMD=-0.71, (95% CI; -1.01, -0.40)], which implies a low 1-minute APGAR score was significantly associated with higher risk for neonatal PTX. The highest risk was found in neonates admitted at the ICU with PTX [SMD=-1.02, (95% CI; -1.69, -0.36)] (Navaei et al., 2010). This is critical since neonatal intensive care studies have demonstrated that PTX is dangerous and necessitates fast chest tube integration based on clinical assessments (Dahmarde et al., 2019). While the lowest risk [SMD=-0.62, (95% CI; -1.04, -0.19)] was recorded among neonates with PTX associated with persistent pulmonary hypertension (Jaroensri et al., 2020).

Many previous studies have demonstrated that variables that had been linked to the development of PTX in newborns (such as birth weight, Apgar score at 1-minute, and surfactant administration) were considered possible risk factors (Dahmarde et al., 2019 & Duong et al., 2014; Masahata et al., 2020). Cut-off values were used to convert birth weight, Apgar scores at 1-minute, best oxygenation index (OI) within 24 hours after birth, and mean airway pressure (MAP) into binary variables. According to the previous research, the ideal cut-off value for birth weight and Apgar score at 1 minute was identified (Dahmarde et al., 2019 & Duong et al., 2014). In contrast, Abdellatif et al., (2012) reported no significant differences in APGAR scores at one and five minutes, as well as the accompanying medical diagnoses, between newborns with PTX who died and those who survived (Garcia-Munoz et al., 2017). Neonatal PTX is more likely in babies who have had prior lung pathology (hyaline membrane disease, mechanical aspiration, and pulmonary infection) that promotes PTX to develop, particularly in premature babies. In the cases with idiopathic PTX and full-term newborn babies, mortality was correspondingly reduced (Abdellatif et al., 2012).

### Strengths & limitations

This is the first systematic review and meta-analysis that investigates the association between APGAR scores and neonatal PTX. We strictly followed the PRISMA guidelines for the conduction process of this study and conducted a comprehensive systematic search. Few studies were available for interpreting the results of this study, so our understanding of these results was restricted.

### Conclusion & recommendations

This study demonstrated a significant association between 1-minute and 5-minutes APGAR scores and neonatal PTX. The highest risk was found among neonates admitted to the ICU and those with persistent PTX. This implies APGAR score is a significant predictor of PTX development and severity. More investigations for further understanding regarding the association between APGAR score and neonatal PTX are required.

### Author contribution

All authors were participating in making study design, data collection, data interpretation and writing all parts of the study. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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**Conflict of Interest**

The authors declare that there are no conflicts of interests.

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**Data and materials availability**

All data associated with this study are present in the paper.

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